PATENT
Docket No. 312762002400

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Dated: 2-2-04 Signature: _____ (Michael Boyd)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In the application of:

Norimitsu SAITO et al.

Serial No.: 09/734,786

Filing Date: December 11, 2000

For: METHODS FOR INTRODUCING GENES INTO MAMMALIAN SUBJECTS

Examiner: D. Sullivan

Group Art Unit: 1636

REPLY BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Appellants file this Reply Brief to Examiner's Answer pursuant to the provisions of 37 C.F.R. § 1.193 in connection with the above-identified application. The Examiner's Answer was mailed on December 2, 2003, according to 37 CFR § 1.193, a Reply Brief must be filed within two months from the mailing of the Examiner's Answer, February 2, 2004. As such, this Reply Brief is timely filed. Herewith, Appellants submit an original and two copies of this reply Brief.

Claims 1-8, 11, 13-15, 17 and 19 of the present application stand rejected under 35 U.S.C. § 112, first paragraph for allegedly lacking enablement. Appellants respectfully request the Board reverse this rejection on the grounds that the Examiner has incorrectly interpreted the subject matter of the pending claims.

I. There is no question that the invention as claimed can be practiced without undue experimentation

The Examiner admits that one of ordinary skill in the art would be able to perform the required steps of the claims of transplanting genetically modified tissue into a subject without undue experimentation (Examiner's Answer, page 3). "The enablement requirement is met if the description enables any mode of making and using the claimed invention." *Engel Industries, Inc. v. Lockformer Co.*, 946 F.2d 1528, 1533 (Fed. Cir. 1991). It is the Examiner's position however, that "the invention is directed to *ex vivo* gene therapy" and that gene therapy is highly unpredictable. (Examiner's Answer, page 5.) In other words, the Examiner has assumed the method of the pending claims must result in a therapeutic effect to be useful. Absent this assumption, there would be no reason to reject the claims for allegedly lacking enablement.

II. Gene therapy is only one of many uses contemplated for the claimed invention

The present specification contemplates a number of uses for the products of the claimed methods besides gene therapy. For example, as the Examiner concedes, the claimed methods can be used to produce a transgenic subject which can then be used as an experimental model to evaluate the effects of administering other substances to the model system (Specification, page 9, lines 1-3). Additionally, the specification contemplates the transplantation of *ex vivo* modified hair follicles to elicit an immune response from a subject transplanted with the modified tissue and to alter hair growth characteristics (Specification, page 4, lines 24 to 28). Any of these asserted utilities is sufficient to make the claimed methods "useful" under the requirements of 35 U.S.C. § 112, first paragraph and 35 U.S.C. § 101.

The claimed methods are useful to produce transgenic animals (Specification, page 9, lines 1 to 3). Transgenic animals were known at the time the present application was filed to be useful for experimentation, for the production of reagents, and for other uses. The present

invention contemplates introducing nucleotide sequences into mammals, such as horses, cows, pigs, sheep, dogs and cats, as well a laboratory animals such as rabbits, mice and rats (Specification, page 9, lines 6 to 15).

Animals produced using the claimed methods have utility, for example as biological assays for candidate compounds effective against a model system (Specification, page 9, lines 1 to 3). The specification also provides guidance regarding how to make and use *ex vivo* modified tissue samples to elicit an immune response from a host (Specification, page 7, line 7 to page 8, line 2). Eliciting an immunogenic response from a host is useful to provide antibodies against a particular gene product and to study the impact of such an immune response on the host organism.

In view of the discussion above it is clear that the present application contemplates a number of possible uses for the claimed invention other than for use in gene therapy.

III. There is no evidence of record that production of transgenic animals, altering hair growth, or eliciting an immune response was unpredictable

The Examiner has alleged that creating transgenic animals was so unpredictable at the time the application was filed that a skilled artisan would need to engage in undue experimentation to make such transgenic animals. However, the Examiner has cited no evidence whatsoever to support this position. In contrast, the teachings of the specification and the level of knowledge available in the relevant art at the time the application was filed.

As discussed in the Appeal Brief, the Examples Section of the application provides detailed guidance to one of ordinary skill in the regarding how to make and use the claimed invention. For example, Example 1 provides a detailed guidance regarding how to culture and genetically modify murine hair follicles. Example 2 provides equally detailed guidance regarding how to transfer genetically modified tissue to a host. The working examples and the other guidance provided in the specification are more than sufficient to teach one of ordinary skill in the art how to make and use the claimed invention. Yet the Examiner has ignored this guidance and repeatedly alleged that the construction of transgenic animals was so unpredictable at the relevant time that the claimed method would require undue experimentation to practice.

The Examiner's position not only ignores the teachings of the specification, it ignores the state of the art at the time the application was filed. Workers in the relevant art were making

transgenic animals and publishing research articles about those animals. This conclusion is supported by the results of a recent search of the literature that yielded thirty-eight (38) different references published on or before December 2000 that discuss the production and use of transgenic animals (See Exhibit A). Applicants hasten to note that the results of this search were narrowed substantially to articles published in late 2000 that related to vertebrate transgenic animals. The large number of references available in this narrow time frame clearly indicates that workers in the relevant art were making transgenic animals without undue experimentation. The lack of any evidence to support the Examiner's position and the showing discussed above demonstrate that making transgenic animals was not as unpredictable as the Examiner alleged.

IV. The Examiner has read a non-existent limitation into the claims

There is absolutely no language recited in the pending claims that requires a therapeutic effect. Nevertheless, the Examiner insists that the pending claims are actually directed to gene therapy and has rejected those claims as allegedly lacking enablement because the specification allegedly does not enable gene therapy. It is Appellants' view that one of ordinary skill in the relevant art would not consider this interpretation of the pending claims to be reasonable.

Claims 1-8, 11, 13-15, 17 and 19 are the subject of the present appeal. Claims 15, 17 and 19 related to an *ex vivo* method of delivering a nucleic acid to a tissue sample, like a hair follicle. Claims 1-8, 11, 13 and 14 relate to the *ex vivo* introduction of a nucleic acid molecule into a tissue, such as a hair follicle, and introducing that tissue into mammalian subject, such as by transplantation. For example, claim 1 reads:

> Claim 1: A method to introduce a nucleic acid molecule into a mammalian subject which method comprises transplanting into the dermis of said subject at least one hair follicle that has been modified ex vivo to contain said nucleic acid molecule.

None of the pending claims contain any language whatsoever that would lead one of ordinary skill in the relevant art to reasonably conclude that the claimed methods require a therapeutic result. Thus, the Examiner has erred in interpreting the pending claims to require a therapeutic result.

Appellants have consistently argued that the pending claims recite no limitations that require a therapeutic result. Instead, the pending claims only recite limitations that definitively and clearly define methods of *ex vivo* transfection and in certain claims, transplantation. In

response, the Examiner has argued that it need not be bound by the ordinary meaning of the claim language but can look to the specification to determine the scope of the claims. The Examiner cites *In re Vogel* to support this proposition. (Examiner's Answer, page 11).

Appellants do not dispute that the Examiner can and should look to the specification to interpret the subject matter of pending claims. "Occasionally the disclosure will serve as a dictionary for terms appearing in the claims, and in such instances the disclosure may be used in interpreting the coverage of the claim." *In re Vogel* 422 F.2d 438, 441 (CCPA 1970). But here, there is no wording identified in the claims that needs such a dictionary.

The Examiner has identified no language within the claims that could be fairly interpreted as requiring a therapeutic effect when practicing the claimed methods. In fact, the Examiner admits that the pending claims are not limited to a therapeutic method (Examiner's Answer, page 12). Yet, the Examiner rests the whole of its enablement rejection of the pending claims on the allegation that the claims require a therapeutic result. Because no language requiring a therapeutic effect explicitly or impliedly appears in the pending claims, it is error on the part of the Examiner to read such a requirement into the pending claims.

Therefore, the present rejection of the claims should be reversed by the Board.

CONCLUSION

The potential uses for the claimed methods are many fold and include the use of the described techniques to practice "gene therapy", alter hair growth, produce transgenic animals, and elicit an immune response. The proffered uses for the claimed invention are each specific, credible, and substantial. Moreover, the specification provides sufficient guidance to allow one of ordinary skill in the art to practice the claimed method without undue experimentation. As such, Applicants have met their burden of providing a sufficient guidance to allow the skilled artisan to make and use the claimed invention without undue experimentation. For the reasons stated above, it is respectfully submitted that the final rejection of claims 1-8, 11, 13-15, 17 and 19 under 35 U.S.C. §112, first paragraph is in error and warrants reversal by the Board.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, appellant petitions for

any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 321762002400. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

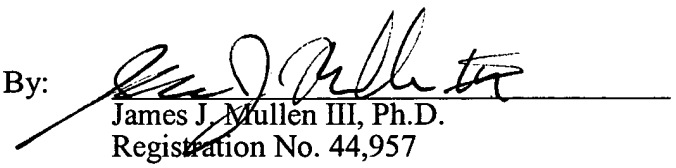
Dated: February 2, 2004 By: 

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Exhibit A

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Respectfully submitted,

Dated: February 2, 2004 By: _____

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